

HCV ADVOCATE WEEKLY NEWS REVIEW

Review of HCV, HBV and HIV/HCV Coinfection Related News and Highlights

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April 19, 2009

Can-Fite BioPharma To Initiate Phase I/II Clinical Trial With CF102 For The Treatment Of Liver Cancer

<http://www.medicalnewstoday.com>

Can-Fite BioPharma (TASE:CFBI), a biotechnology company traded on the Tel Aviv Stock Exchange announced that, following the approval by the Israel Ministry of Health and Rabin MC Ethics Committee, a phase I/II clinical trial with **CF102** for the treatment of liver cancer will now start enrolling patients.

The trial will investigate the safety and efficacy of CF102 in patients with liver cancer. This ascending-dose trial will be conducted at the Rabin Medical Center and include up to 40 patients.

Liver cancer is one of the five most common types of cancer globally, accounting for about 450,000 new diagnoses each year, and is highly prevalent in individuals with hepatitis B and C virus infection and in alcohol users. This type of cancer, which currently has no effective treatment, is particularly prevalent in Eastern countries. The chemotherapies that benefit patients with other types of cancers fail to affect liver cancer. The market potential of such a drug may be up to billions of dollars.

Can-Fite is currently planning to develop CF102 for liver disease, including but not limited to liver cancer and hepatitis C. CF102, which is based on Can-Fite's technological platform, is a targeted drug that binds to the A3 adenosine receptor with high affinity.

This receptor is highly expressed on the surface of cancer and inflammatory cells but not on healthy cells. CF102 binds its target on affected cells and leads to apoptosis (programmed cell death). Preclinical trials have shown that CF102 is effective for the treatment of liver cancer.

In keeping with its financial reports, Can-Fite expects to release within weeks the results of a phase IIB clinical trial with CF101 for the treatment of rheumatoid arthritis and a phase IIA

clinical trial with CF101 for the treatment of Dry Eye Syndrome.

Prof. Pnina Fishman, CEO of Can-Fite, said today that "CF102 represents another application of the unique technology developed by Can-Fite for cancer and inflammatory diseases. According to our tests, this technology is particularly appropriate for the treatment of liver cancer, which is currently considered to have very low chances of recovery and presents a massive global need for a cure."

CAN-FITE BIOPHARMA LTD is a public company traded on the Tel Aviv Stock Exchange. The Company, which commenced business activity in 2000, was founded by Prof. Pnina Fishman, an investigator from Rabin Medical Center, and patent attorney Dr. Ilan Cohn, a senior associate at Reinhold Cohn Patent Attorneys. Prof. Pnina Fishman serves as the CEO of Can-Fite. The Company was founded on the basis of scientific findings made by Prof. Pnina Fishman and focuses on the development of molecule-based drugs that bind to receptors on and inhibit the development of cancer or inflammatory cells.

Can-Fite's development pipeline currently has two drugs, CF101 and CF102. The company is simultaneously conducting several preclinical and clinical trials with the two drugs for various indications. CF101 is being studied for the treatment of rheumatoid arthritis, dry eye syndrome and psoriasis. Can-Fite has also entered the development of CF102 for the treatment of liver cancer, including liver cancer, hepatitis virus infections and liver tissue regeneration.

Source: Can-Fite Biopharma LTD

April 20, 2009

Transplanted Liver Cells Function In Older Animals But Do Not Proliferate As Much As In Younger Ones

<http://www.medicalnewstoday.com>

When things go right, healthy liver cells transplanted by infusion or injection will find their way to the liver, integrate into the damaged tissue, start proliferating, and take over the liver's work of helping with digestion and removing waste products and worn-out cells from the blood. Hepatocyte transplantation has been successful in a number of animal models, raising hopes that use of cells could overcome the shortage of donor livers and the problems of surgery, but the procedure has not been as successful in humans. Was the problem related to the age of the donor?

Now scientists at the Martin Luther University Hale-Wittenberg, Germany, believe they know the answer. Age of the donor makes no difference but age of the recipient makes a big one. Many humans requiring liver transplantation are older. The German study conducted in rats found that older rats had a repopulation rate of only 2 percent, ten times less than that seen in younger ones. Furthermore, found the scientists, the transplanted cells worked equally well in the old and young animals, as measured by glycogen storage, but the younger animals had significantly higher levels of a growth factor needed for proliferation.

The new study is the first to offer a possible mechanism for the failure of transplanted hepatocytes to proliferate in many human patients - and the first to suggest a way to compensate

for the problem. Dr. Peggy Stock, a postdoctoral fellow in the laboratory of Dr. Bruno Christ, reported the study on April 19 at Experimental Biology 2009 in New Orleans. The presentation was part of the scientific program of the American Society for Investigative Pathology.

The researchers isolated hepatocytes from both four week old rats (the equivalent age of a human child) and rats more than 35 weeks old (40 to 50 years in humans). These healthy liver cells were then implanted into the livers of young rats (10 weeks, the equivalent of young adulthood) and "senescent" rats (more than 35 weeks).

After six weeks, the amount of hepatocyte proliferation was determined by an assay of CD26 enzyme activity. The recipient animals had been bred to lack the CD26 protein, giving the researchers a way to determine which and how many liver cells were part of the recipient liver and which had the CD26 gene product, indicating they originated from the transplant.

Repopulation of hepatocytes was 20 percent in young rats, whether the cells came from a young or old donor. In older rats, by contrast, repopulation was only 2 percent.

All the transplanted and proliferated cells worked, whether they were transplanted into old or young rats and whether they came from old or young rats. However, IGF1 (insulin like growth factor 1, which regulates growth in the liver and other organs) was significantly higher in the juvenile rats.

The next step, say Dr. Stock and Dr. Christ, is to inject IGF1 in old rats and see if this pretreatment would increase the proliferation levels of hepatocyte cells.

Co-authors of the study, in addition to Dr. Stock and Dr. Christ, are Sabine Ebensing and Madlen Hempel, also of the First Department of Internal Medicine, Martin Luther University Halle-Wittenberg, and Dr. Maximilian Bielohuby and Dr. Martin Bidlingmaier, of the Department of Endocrinology, Maximilian Ludwig University, Munich. Funding for the research comes from the German Ministry of Education and Research and the German Research Foundation.

Source: Sylvia Wrobel, Federation of American Societies for Experimental Biology

Stressed Americans postpone healthcare

www.reuters.com

WASHINGTON (Reuters) - Twenty percent of Americans say they have delayed or postponed medical care, mostly doctor visits, and many said cost was the main reason, according to a survey released on Monday.

The Thomson Reuters survey found 21 percent of U.S. adults expected to have difficulty paying for health insurance or healthcare services in the next three months.

"The results of this survey have serious implications for public health officials, hospital administrators, and healthcare consumers," Gary Pickens of the Healthcare division of Thomson Reuters, who led the study, said in a statement.

"We are seeing a positive correlation between Americans losing their access to employer-sponsored health insurance and deferral of healthcare."

Pickens added that "if this trend continues, it will ultimately have an impact on our collective well-being."

Thomson Reuters Healthcare is part of the same company as the Reuters news agency.

Pickens and colleagues surveyed 12,000 Americans in February and March and said their findings were representative of the United States in general.

They found that 24 percent of people who canceled or postponed care said cost was the primary reason.

In 2006, the last time the question was asked on the survey, 15.9 percent of people said they had postponed or canceled medical care in the past year.

More than 54 percent who skipped care said they missed a doctor visit. Eight percent said they delayed or skipped medical imaging of some sort.

Pickens and colleagues found the percentage of households with employer-sponsored insurance declined to 54.6 percent in 2009 from 59 percent in early 2008. The percentage of adults covered by Medicaid, the state-federal health insurance plan for the poor, rose to 14.5 percent in 2009 from 11.9 percent in 2008.

(Reporting by Maggie Fox; Editing by Peter Cooney)

Pharmasset stops hepatitis B trial, shares drop

www.reuters.com

BANGALORE, April 20 (Reuters) - Pharmasset Inc (VRUS.O) said it stopped a late-stage study of its experimental treatment for chronic hepatitis B [**clevidine**] due to several serious adverse events in patients receiving the drug, sending its shares down 17 percent.

However, analysts said discontinuing the hepatitis B trial could be a "long-term gain," as it would let the company channel all its resources to its more watched-out hepatitis C pipeline.

The company, which decided to stop the trial named QUASH after a discussion with its independent data monitoring committee and the U.S. Food and Drug Administration, said it would now focus its resources on its hepatitis C pipeline.

"Few investors had given the company much credit for the drug for hepatitis B and were investing in the company almost entirely based on the prospects of its hepatitis C drugs," Canaccord Adams analyst Adam Cutler said.

The company said it recently became aware of a number of spontaneous serious adverse event reports in patients receiving the drug, clevidine, as prescribed therapy for hepatitis B in South

Korea.

Clevudine, the company's most advanced drug candidate, was licensed from Bukwang Pharmaceuticals Co Ltd (003000.KS) of South Korea, where the drug is marketed under the trade name Levovir.

"You never really want to see a company stopping a late-stage trial, but at the end of the day they are going to save a lot of money in launch and commercialization costs," JMP Securities analyst Liisa Bayko said.

"I think that dollar would be better utilized on hepatitis C and there would be better return on investment for those dollars spent," Bayko added.

Canaccord Adams analyst Adam Cutler said a lot of Pharmasset's research and development spending was going to fund Clevudine, so discontinuing that program would give it a longer cash runway, "an important characteristic for any company these days."

Pharmasset plans to collect safety data and to monitor patients after the discontinuation of the trial, but does not plan to submit study results to regulators as pivotal studies.

Hepatitis B and hepatitis C are potentially fatal liver diseases that can lead to cirrhosis and liver cancer.

Pharmasset's lead hepatitis C candidate, R7128, was slated to start a mid-stage trial in the first quarter of 2009. It plans to start an early stage clinical study on another experimental hepatitis C treatment, PSI-7851.

Shares of the company were trading down 12 percent at \$8.10 Monday morning on Nasdaq. They had touched a low of \$7.69 during the session.

Needle-exchange worker helps heroin users in Rock County

<http://gazettextra.com>

By Frank Schultz

Jimi Reinke is in Rock County twice a week distributing syringes to drug users.

He is doing nothing illegal. His job is to keep people from dying from dirty needles.

Reinke works for Lifepoint Needle Exchange, a program of the AIDS Resource Center of Wisconsin. Based in Madison, he works a territory from the Dells south to the state line.

Rock County is a prime territory.

He figures he gives out 2,000 syringes a week, 800 of those in Rock County.

That works out to more than 40,000 needles a year in Rock County, and Reinke is not the only source for local drug users.

Most of those syringes are used for heroin, Reinke said.

Reinke has seen a change in the drug-using population here. It used to be much older.

“Then two years ago, I connected with these kids in Janesville,” Reinke said. “There’s so many of them who are 17 to 22. It’s like, if you know a 20-year-old in Janesville, they know someone who shoots heroin.”

The same trend—younger users, including affluent suburbanites—is seen in other Wisconsin cities in recent years, said Scott Stokes, public affairs director for the AIDS resource center.

Reinke said Rock County is well positioned for heroin users. The supply comes from the south, mostly Rockford, Ill. A dose that costs \$10 in Rockford could cost \$20 to \$30 in Madison and \$50 to \$70 in the Wisconsin Dells, Reinke said.

Rock County Sheriff Bob Spoden said he appreciates the fact that needle exchanging limits HIV exposure, but he is concerned it also might legitimize heroin use.

The sheriff’s office wants to put needle exchange programs out of business by taking away their customers, Spoden said.

Reinke said he doesn’t encourage drug use. In fact, he will encourage drug users to get help if they seem receptive.

But often, treatment is hard to find or to pay for, and it’s easier to go back to using, Reinke said.

Stokes said Lifepoint is probably the largest needle-exchange program in the country, and one of the most successful. New HIV infections from drug use have declined 67 percent since the program started, he said.

Reinke started coming to Beloit nine years ago. Now he’s in Janesville or other towns just as often.

“It’s really all the towns in Rock County—Milton, Edgerton,” he said.

Reinke would not allow his photo to be taken because being identifiable on the street could jeopardize the trust that drug users place in him.

Users call Reinke. He’ll come to them—to a house, a park or a parking lot, he said.

Reinke’s work includes distributing little metal “cookers” and cotton balls that are used to clean sediments out of the heroin before it is injected. A used cooker could harbor infected blood.

He also hands out cards with phone numbers and flyers about drugs and infections.

Another item in Reinke carries is Narcan, a drug that blocks the body’s opiate receptors. An injection of Narcan can prevent someone from dying from a heroin overdose.

Reinke has trained more than 200 people how to use Narcan, and he's heard of 224 times that it's been used in the 2 1/2 years he's been giving it out.

EMTs and paramedics carry Narcan as well.

Reinke tries to train drug users: Never use alone. The same amount of heroin in a packet might get you high, might not be enough to get you high, or could be so potent that it could kill you, Reinke advises.

That's where the Narcan comes in.

Some users tell their friends never to inject them with Narcan, however. The Narcan will interrupt the pleasure and put them into withdrawal, Reinke said. They'd rather take the chance that they might die than to stop the high.

Heroin users often don't know the dangers of dirty needles before Reinke tells them. They might not know, for example, that HIV will die when the blood dries, but the hepatitis C virus doesn't.

Hepatitis C is "just rampant" among people who inject drugs, Reinke said. While HIV is still around, hepatitis C is "five times the epidemic," he said.

Users know they can get busted for having a dirty needle, which the law considers drug paraphernalia. Clean needles are legal, however, so users are motivated to exchange used syringes for Reinke's clean syringes.

Reusing needles also can cause ugly wounds, infections and scars.

"The first time you use it, it's bent," Reinke said. "The second time it's a barb, and the third time you're tearing yourself up."

Reinke has seen pus-filled arms that had to be cut open and drained at the hospital.

Reinke also distributes antibiotic ointment and vitamin E capsules, which help the wounds heal.

Summaries For Patients: Re-treating Patients With Chronic Hepatitis C Who Have Not Responded to Peginterferon-2b

<http://www.annals.org>

21 April 2009 | Volume 150 Issue 8 | Page I-34

The summary below is from the full report titled "Re-treatment of Patients With Chronic Hepatitis C Who Do Not Respond to Peginterferon-2b. A Randomized Trial." It is in the 21 April 2009 issue of *Annals of Internal Medicine* (volume 150, pages 528-540). The authors are D.M. Jensen, P. Marcellin, B. Freilich, P. Andreone, A. Di Bisceglie, C.E. Brandão-Mello, K.R. Reddy, A. Craxi, A. Oliveira Martin, G. Teuber, D. Messinger, J.A. Thommes, and A. Tietz.

What is the problem and what is known about it so far?

Hepatitis C is inflammation of the liver caused by the hepatitis C virus (HCV). This disease is

transmitted primarily by blood-to-blood contact. Risk factors include body piercing, intravenous drug use, and needlestick accidents. Most people cannot get rid of HCV on their own. More than 80% keep the virus in their blood for longer than 6 months and get chronic hepatitis C.

Chronic hepatitis C progresses slowly over 10 to 30 years. It causes inflammation and scarring of the liver. If untreated, it can lead to liver failure and liver cancer. Treatment clears HCV from the blood and prevents further liver damage. Doctors treat chronic hepatitis C with powerful antiviral drugs. They often combine a long-acting immunity-boosting protein (pegylated interferon) with another antiviral drug (ribavirin). However, the virus does not clear after initial treatment in about 20% to 30% of patients. We do not know whether re-treating them improves outcomes.

Why did the researchers do this particular study?

To see whether any of 4 regimens improves viral outcomes in patients with chronic hepatitis C who had not responded to previous combination therapy.

Who was studied?

950 patients with chronic hepatitis C. None had responded to previous treatment with peginterferon-2b plus ribavirin.

How was the study done?

Researchers randomly assigned patients to 1 of 4 groups. The groups received peginterferon-2a for 48 or 72 weeks and either fixed-dose induction or standard-dose peginterferon regimens. The fixed-dose induction was 360 µg/wk for 12 weeks followed by standard 180-µg/wk doses. All patients took standard doses of ribavirin (1000 to 1200 mg) by mouth daily. The researchers measured levels of virus in the blood regularly during re-treatment and 24 weeks after re-treatment ended. They routinely did blood tests, physical examinations, and interviews to check for side effects. They then assessed which re-treatment regimen got rid of the virus most often.

What did the researchers find?

Patients who were re-treated for 72 weeks had sustained virologic response after treatment ended more often than did those who were re-treated for 48 weeks (16% vs. 8%). The dose of peginterferon-2a that was given during the first 12 weeks of re-treatment did not affect response rates much. Undetectable virus levels at week 12 seemed to identify the patients who were most likely to respond to re-treatment. More patients in the longer-duration treatment groups withdrew from the trial because of adverse events or illnesses than did those in the shorter-duration treatment groups (12% vs. about 5%).

What were the limitations of the study?

Researchers and patients knew which therapies the patients received. Only nonresponders to a peginterferon-2b plus ribavirin regimen were studied.

What are the implications of the study?

Re-treating patients who had not responded to previous therapy for chronic hepatitis C for a longer rather than a shorter duration improved viral response. Sustained virologic response rates, however, were low. A positive aspect is that responders could be identified as early as week 12.

Are TACE Treatments Really Well Tolerated Without Any Sensible Reduction Of Liver Function?

<http://www.medicalnewstoday.com>

Recently, it has been demonstrated that TACE improves survival compared with best supportive care in meta-analyses of randomized trials and in two individual clinical trials. However, although selective where TACE is currently widely used, there are no reported extensive data from large series on both short and long term effects of this treatment on liver function. Equally, because the optimal number of sessions is not known, it is debatable if repeated courses of selective TACE may progressively impair liver function and if they are well tolerated or are limited by major side effects.

A research article published on April 21, 2009 in *World Journal of Gastroenterology* addresses this question. The research group, guided by Dr. Sacco from the Gastroenterology Department of Pisa University Hospital, has performed a prospective cohort study on a large group of patients affected by HCC, prospectively evaluating the short and long term impact of selective TACE on liver function. Side effects of treatments were also assessed and the overall survival and progression free survival probabilities were analyzed.

This single center study is very interesting because it evaluates, in a very large population of patients, the effective clinical impact of TACE procedure. This technique, although not included in the number of curative techniques for HCC, has proved to be efficacious in prolonging life expectancy in patients affected by primary liver cancer. Nevertheless many questions remain a matter of debate: how many times can we repeat this treatment without reducing liver function? Is there any difference between multitreated patients and subjects at the first treatment? What is the real life expectancy and HCC progression free survival probability?

This study demonstrates that in a two year period with a well selected population of HCC patients, TACE treatments are really well tolerated without any sensible reduction of liver function, with a low rate of side effects and complications and excellent survival perspectives. One of the most interesting parameters evaluated is the HCC progression free survival probability: the excellent results (69% at two years) confirm the efficacy of this treatment with more than two thirds of patients in a stable clinical condition at the end of the study period. The proper selection of candidates for TACE appears to be a key point in this study: even if a consensus has not yet been reached, the best candidates for TACE seem to be asymptomatic patients with preserved liver function without vascular invasion or extrahepatic tumour spread. Patients suitable for TACE were selected using Child-Pugh, CLIP and BCLC staging systems: these scoring systems have been developed in the past years in order to achieve the best predictive power. In this study these systems are used in conjunction and results obtained seem to demonstrate that this is a real prospect for the future. TACE was repeated "on demand", when there was evidence of insufficient tumor response, tumor recurrence or disease progression. According to data shown, this type of treatment schedule may help preserving liver function and can be well tolerated in elderly patients, often suffering from co-morbidities, as well as in patients previously treated with other therapeutic techniques.

In conclusion, on the basis of Dr. Sacco study results, in a strict selected patient population,

TACE is a safe and efficacious procedure in the treatment of hepatocellular carcinoma. At this time, further studies are warranted to consider the clinical impact of new methods of chemoembolization using drug-eluting particles, which could allow larger tumor necrosis with reduced systemic effects.

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Sacco R, Bertini M, Petruzzi P, Bertoni M, Bargellini I, Bresci G, Federici G, Gambardella L, Metrangolo S, Parisi G, Romano A, Scaramuzzino A, Tumino E, Silvestri A, Altomare E, Vignali C, Capria A. Clinical impact of selective transarterial chemoembolization on hepatocellular carcinoma: A cohort study. *World J Gastroenterol* 2009; 15(15): 1843-1848
<http://www.wjgnet.com/1007-9327/15/1843.asp>

Correspondence to: Rodolfo Sacco, MD, PhD, Gastroenterology Department, Pisa University Hospital, Via Paradisa 2, 56124 Pisa, Italy.

Source: Lin Tian, World Journal of Gastroenterology

Early treatment gives hepatitis C patients the all-clear

<http://www.theaustralian.news.com.au>

Leigh Dayton
The Australian

THERE is good news for people with hepatitis C, say medical researchers who have found that with early treatment up to 70 per cent of patients will be cured of the debilitating infection.

What's more, the international team showed that, overall, when treating the blood-borne virus, the standard combination drug treatment was as effective as a stronger regimen, which caused more serious side effects.

According to the advocacy body Hepatitis Australia, more than 200,000 Australians have chronic hepatitis C. Nationwide, more than 278,000 are exposed to the virus, primarily through use of needles with traces of infected blood. The group estimates that less than 2 per cent of infected people receive treatment.

Without treatment people would eventually develop serious liver disease, said research leader, hepatologist Stuart Roberts, director of gastroenterology and hepatology at The Alfred hospital in Melbourne.

"A cure will prevent the development of liver disease," he said.

Professor Roberts said hepatitis C was the main reason for liver transplants in Australia, "is a health burden and (causes) loss of time at work and an impaired quality of life".

The new results come from the so-called CHARIOT study, an international randomised control trial involving 702 Australian patients and 194 from New Zealand, Canada, Thailand, Argentina and Mexico. All had the most difficult type of hepatitis C to treat, hepatitis C genotype 1.

James Kellner, 42, was one of the Australian patients. Having learned that a bone marrow transplant and blood transfusions for leukemia had left him with the virus, he volunteered for the trial. He is now cured.

"The 11-month treatment was quite hard but it was definitely worth it to know the disease is gone," he said.

Professor Roberts said that because the disease could have no symptoms, anyone who engaged in risky behaviour or had been treated with blood products prior to 1990 should be tested. He said Mr Kellner's good outcome reflected the CHARIOT finding that early treatment with a combination of interferon, to slow viral replication, and the antiviral drug ribavirin, was effective.

Professor Roberts will present the findings next Saturday at the congress of the European Association for the Study of the Liver, in Copenhagen. Details will be published in the journal *Hepatology*.

April 22, 2009

U.S. consumer group, drug companies want Medicaid expanded

www.reuters.com

SizeBy Lisa Richwine

WASHINGTON (Reuters) - A leading consumer group and a trade association representing major drug companies said on Tuesday they would spend millions to promote three changes to the U.S. healthcare system, including expanding government insurance for the poor.

Families USA and the Pharmaceutical Research and Manufacturers of America (PhRMA) said they would launch a multimillion-dollar advertising and lobbying campaign to get lawmakers to expand Medicaid insurance to more people, provide subsidies for moderate income individuals and families to buy insurance and cap out-of-pocket expenses for low- and middle-income people with insurance.

Ron Pollack, executive director of Families USA, said at a news conference with PhRMA chief Billy Tauzin that the groups, often on opposite sides of issues, had found areas of agreement that were "designed to make sure nobody's left out of the system."

Families USA has attacked drugmakers' prices and advocated importation of cheaper medicines and other policies opposed by PhRMA, which represents Pfizer Inc, GlaxoSmithKline PLC and Merck & Co Inc and other companies.

Despite lingering differences on some major issues, Tauzin said there was "a lot of common ground."

Soaring health care costs, rising unemployment and millions of uninsured Americans are putting pressure on lawmakers to reform the health care system in the United States.

PhRMA and Families USA did not address a major question facing lawmakers about whether a

government-run plan would be part of the mix of insurance options that will be available to Americans.

Democrats want a public plan, but insurers and Republicans argue that private companies would be unable to compete with a potentially cheaper government-run option.

Senate Democrats who are drafting health insurance legislation are aiming to have bills ready for consideration by early June.

Drugmakers could expand their markets if more people had health insurance, but they could also face government efforts to lower drug prices.

Tauzin said pharmaceutical companies were concerned about a call for lower drug prices in Medicaid, which he called "an extremely regulated area of healthcare" that needed changes.

(Reporting by Lisa Richwine; Editing by Toni Reinhold)

Biolex Therapeutics Commences Phase 2B Trial Of Locteron(R) In Chronic Hepatitis C

<http://www.medicalnewstoday.com>

Biolex Therapeutics, Inc. announced the commencement of patient dosing in the SELECT-2 Phase 2b trial of its lead product candidate Locteron for the treatment of chronic hepatitis C. Locteron, controlled-release interferon alpha 2b, is designed to improve patient care by providing a more convenient once-every-two week dosing schedule and by reducing the side effects associated with pegylated interferons, the current standard of care, including flu-like symptoms. The Company also announced that the preliminary results of the recently completed United States Phase 2a Locteron trial ("PLUS" trial) will be presented at the 44th Annual Meeting of the European Association for the Study of the Liver (EASL) April 24, 2009 in Copenhagen, Denmark.

The Phase 2b trial is being conducted in the United States and Europe in 100 treatment-naive, genotype-1, chronic hepatitis C patients. Patients will be randomized into one of four dosing cohorts, the 320, 480 or 640 ug dose of Locteron (administered once every two weeks) or a control arm consisting of PEG-Intron(R) (administered every week), with all patients receiving weight-based ribavirin. Patients will be treated for 48 weeks and will be followed for an additional 24 weeks to determine the sustained virologic response (SVR) rate. The interim results after 12 weeks of treatment are expected to be used as the basis for the selection of the Locteron dose(s) for Phase 3 trials.

"The primary objective of the SELECT-2 Phase 2b trial is to identify one or more doses of Locteron for advancement to Phase 3 trials based on an evaluation of viral response and safety and tolerability, including reductions in flu-like symptoms," said Mr. Jan Turek, Biolex's President and Chief Executive Officer. "We believe Locteron to be a valuable asset as it is the only controlled-release interferon alpha under development, and interferon alpha serves as the current standard of care for hepatitis C and provides the backbone for each of the new anti-viral candidates under development. Market research confirms that there is a substantial commercial

opportunity for Locteron if a tolerability advantage is demonstrated in more advanced clinical testing."

Locteron is an investigational therapeutic candidate and has not been approved for sale by the United States Food and Drug Administration or by any international regulatory agency.

Locteron Overview

Locteron is a controlled-release interferon alpha designed to improve patient care in the treatment of hepatitis C through a more favorable side-effect profile and dosing convenience compared to existing pegylated interferon products. In contrast to Locteron's controlled-release mechanism, the currently approved products, Pegasys(R) and PEG-Intron(R), and the investigational product Albuferon(R), are immediate-release products that lack a controlled-release mechanism. Interferon alpha serves as the foundation of current combination therapy for hepatitis C patients, and all major hepatitis C drug candidates currently in clinical trials are being studied in combination with interferon alpha. It is estimated that worldwide sales of interferon products for the treatment of hepatitis C will approach \$6 billion by 2016.

Locteron combines BLX-883, a recombinant interferon alpha produced by Biorex in its patented LEX System(SM), with PolyActive(R), an advanced controlled-release drug delivery technology developed by OctoPlus N.V. of Leiden, the Netherlands. Locteron is configured to allow dosing once every two weeks, more convenient than Pegasys(R) and PEG-Intron(R), each of which require dosing every week. More importantly, Locteron's controlled-release mechanism results in the gradual release of interferon alpha 2b to patients over the duration of two weeks and avoids the early peak plasma levels of the active interferon that characterize the pegylated interferons and Albuferon. This controlled-release mechanism is designed to reduce the frequency, duration and severity of side effects, including flu-like symptoms, commonly experienced by patients treated with pegylated interferons and with Albuferon. The Company has completed three clinical trials of Locteron, and the results of the SELECT-1 Phase 2a trial were presented at the 43rd Annual Meeting of the European Association for the Study of the Liver in April 2008.

Source: Biorex Therapeutics

INFORM-1 Clinical Trial Amended To Further Explore Promising Direct Antiviral Regimen In HCV Patients

<http://www.medicalnewstoday.com>

InterMune, Inc. (Nasdaq: ITMN) announced that the innovative clinical study of protease inhibitor **ITMN-191 (R7227)** in combination with nucleoside polymerase inhibitor **R7128** (Roche/Pharmasset), referred to as the INFORM-1 study, has been successfully amended to include additional cohorts to explore the combination in treatment-experienced and null responder HCV patients. In addition, the amended protocol now includes the administration of twice-daily and higher-dose regimens of ITMN-191 in combination with R7128 in treatment-naive patients.

Dan Welch, Chairman, Chief Executive Officer and President of InterMune, said, "The first four cohorts of the INFORM-1 study successfully demonstrated that the novel combination of relatively low doses of two direct antiviral agents can be administered safely and, in the absence

of interferon, result in robust antiviral activity in treatment-naive HCV patients. INFORM-1 has now been expanded to explore this novel regimen in treatment-experienced patients; both non-responder patients and so-called null responders, which together represent an important unmet medical need as their treatment options are currently very poor. The inclusion of twice-daily dosing of ITMN-191 at doses of up to 900mg, doses that were safely and effectively explored when combined with the current standard of care, is another important expansion of INFORM-1. We look forward to the results of these important new cohorts."

INFORM-1 Expanded Study Design

The expanded INFORM-1 design now includes three additional dosage cohorts, Cohorts E, F and G, as follows:

- Cohort E evaluates the combination of twice-daily doses of ITMN-191 (600mg) and twice-daily R7128 (1000mg), or placebo, for 14 days in treatment-experienced patients with genotype 1 HCV infection who have been previously treated with pegylated interferon plus ribavirin, but did not achieve a sustained virologic response (SVR).
- Cohort F consists of null responder HCV patients with genotype 1 infection who have been treated with pegylated interferon plus ribavirin, but experienced a null response. Null response is defined as experiencing <2.0 log₁₀ decline in HCV RNA at week 12, and/or <1.0 log₁₀ decline at week 4. Patients will be administered twice-daily doses of ITMN-191 (900mg) and twice-daily R7128 (1000mg), or placebo, for a period of 14 days.
- Cohort G enrolls treatment-naive patients who will be administered twice-daily doses of ITMN-191 (900mg) and twice-daily R7128 (1000mg), or placebo, for a period of 14 days.

INFORM-1 Initial Study Design

The INFORM-1 study was initially designed to evaluate the safety and combined antiviral activity of ITMN-191 and R7128 in 14 days of combination therapy in treatment-naive patients chronically infected with HCV genotype 1. The original study protocol consisted of four dosage cohorts -- Cohorts A, B, C and D -- comprised of a total of six dosing groups:

- Cohort A consists of two dosing groups, Group A and Group B. Patients in Group A receive 500mg BID of R7128 as monotherapy for three days, followed by four days of combination therapy comprised of the same dose of R7128 plus 100mg q8h of ITMN-191. Patients in Group B receive 100mg q8h of ITMN-191 as monotherapy for three days followed by four days of combination therapy comprised of the same dose of ITMN-191 plus 500mg BID of R7128.
- Patients in Cohort B (Group C) receive the same doses of R7128 and ITMN-191 as in Cohort A, but for 14 days in combination.
- Cohort C consists of two dosing groups, Group D and Group E. Patients in Group D receive 1000 mg BID of R7128 and 100mg q8h of ITMN-191 for 14 days. Patients in Group E receive 500 mg BID of R7128 and 200 mg q8h of ITMN-191 for 14 days.
- Patients in Cohort D are dosed in one Group (Group F) and receive 1000 mg BID of R7128 and 200 mg of ITMN-191 q8h for 14 days.

About INFORM-1

The INFORM-1 clinical trial, being conducted in centers in Australia and New Zealand, is the first to investigate the combination of two oral direct-acting antiviral medicines in the absence of interferon. This initial study was designed to evaluate the safety and combined antiviral activity

of R7227 (ITMN-191), a protease inhibitor, and R7128, a polymerase inhibitor, in 14 days of combination therapy.

This direct-acting antiviral combination study represents an important first step in evaluating the therapeutic potential of an all-oral, interferon-free combination treatment for HCV. With InterMune, Roche is developing ITMN-191 (R7227), an HCV protease inhibitor compound to be used in combination with PEGASYS(R) (peginterferon alfa-2a) and COPEGUS(R) (ribavirin), the current standard of care. Concurrently with Pharmasset, Roche is developing R7128, an HCV RNA polymerase inhibitor, also for therapy in combination with PEGASYS(R) and COPEGUS(R). Both of these molecules have successfully completed Phase 1b monotherapy studies, have been dosed in combination with PEGASYS(R) and COPEGUS(R) and both have individually demonstrated safety and robust antiviral activity in HCV patients.

Current standard of care for HCV comprises pegylated interferon plus ribavirin, for a duration that is dependent upon factors such as genotype of the virus. For the most difficult to treat genotype 1 virus, a 48-week treatment course generally results in sustained viral response in about 50% of patients.

An abstract of interim results from the INFORM-1 study (Cohorts A and B) has been accepted for an oral late-breaker presentation at the 44th Annual Meeting of the European Association for the Study of the Liver (EASL), to be presented on Saturday, April 25 at the EASL meeting in Copenhagen, Denmark.

Source: InterMune, Inc

ImQuest BioSciences Receives Phase I SBIR Grant To Develop A Novel Hepatitis C Virus Therapeutic Agent

<http://www.medicalnewstoday.com>

ImQuest BioSciences and Arisyn Therapeutics jointly announced the successful acquisition of funding from the National Institutes of Health to support the development of novel small molecule therapeutics for the treatment of hepatitis C virus (HCV) infection. ImQuest scientists will investigate the therapeutic potential and mechanism of action of **ATI-0810** (*Formerly PG301029*) and a series of related chemical compounds. PG301029 is a highly novel transcriptional inhibitor of HCV replication, yielding a significant reduction of viral RNA synthesis in infected cells, and laboratory studies have demonstrated the compound to be less toxic and more active than the FDA approved agent ribavirin. Preliminary in vivo toxicology studies indicate that the compound is well tolerated and has a pharmacokinetic profile appropriate for drug development. The ImQuest research team will be led by Principal Investigator Todd B. Parsley, Ph.D., Director of Hepatitis Virus Research. The funded studies will permit ImQuest to define other potent transcriptional inhibitors of HCV, investigate the mechanism of action of the active molecules and provide additional rationale for the development of a combination anti-HCV therapy using the lead molecules.

"We believe that the addition of a novel agent such as PG301029 to the current standard of care for HCV infected individuals will greatly enhance the percentage of patients that are able to achieve a robust and durable antiviral response to therapy," said Dr. Robert W. Buckheit, Jr.,

Executive Vice President of ImQuest. "Our data provide adequate rationale for the expedited development of PG301029 for HCV infection, and provide a platform to identify novel cellular and viral targets for future antiviral therapeutic development efforts."

The research continues the collaborative scientific partnership between ImQuest and Arisyn Therapeutics for the development of Arisyn Therapeutic's portfolio of antiviral and anticancer products.

ImQuest BioSciences Inc. is a privately held U.S. company located in Frederick, Maryland, is a leading provider of anti-infective therapeutic and microbicide development services to the biotechnology and pharmaceutical industry.

Arisyn Therapeutics Inc. is a privately held virtual biotechnology company headquartered in Frederick Maryland with a mission of identifying novel first in class inhibitors for infectious diseases and cancer based on their transcription targeted therapeutic agent platform.

Source: ImQuest BioSciences Inc

Re-Treatment With Pegasys(R) Provides Hepatitis C Patients With A Second Chance For A Cure, Switzerland, New Study

<http://www.medicalnewstoday.com>

New data published in a major peer-reviewed journal, *Annals of Internal Medicine*, show that re-treatment with Pegasys(R) (peginterferon alfa-2a) plus Copegus(R) (ribavirin) provides previously-treated hepatitis C patients a second chance for a cure. The study results demonstrated that patients most likely to respond to re-treatment could be identified after only 12 weeks, allowing patients and their doctors to be confident early on about the likelihood of success.(1)

"While tremendous advances in hepatitis C treatment have cured many hepatitis C patients, a significant proportion of patients do not achieve success with their first treatment course. This is leading to a large and growing population of patients who are in urgent need of alternative treatment options," said Donald Jensen, US principal investigator for REPEAT, and Professor of Medicine and Director of the Center for Liver Diseases at the University of Chicago Hospital in Chicago. "With 72 weeks of Pegasys and ribavirin combination treatment as a new solution for those with the most difficult-to-treat form of the virus, patients can now feel more hopeful that they have the possibility to achieve a cure when previous therapy has failed."

Pegasys (peginterferon alfa-2a) received European Commission approval for the re-treatment of hepatitis C in December 2008, based in part on results of the newly-published study. For patients with genotype 1 virus who were initially treated with pegylated interferon and ribavirin, it is recommended that they be retreated with peginterferon alfa-2a for an extended period of 72 weeks. Peginterferon alfa-2a is now the first and only pegylated interferon to be approved anywhere for treatment of up to 72 weeks. For all other previously-treated patients, the recommended treatment period is 48 weeks.

The Need for Re-treatment Options

The standard of care for patients with chronic hepatitis C is the combination of a pegylated

interferon plus ribavirin. In hepatitis C, sustained virologic response (SVR) to interferon-based treatment is widely equated to cure(2) as it is associated with eradication of HCV infection and improvement in liver disease. Approximately 50% of patients with genotype 1, the most difficult to treat form of the disease, and 20-30% of patients with genotypes 2 or 3 do not achieve a cure after a first course of therapy.(1)

The REPEAT Study

Enrolling 950 patients from Europe, North America and Latin America, the REPEAT (REtreatment with PEGasys in pATients Not Responding to Peg-Intron Therapy) study was designed to explore whether intensified treatment with a higher initial dose of Pegasys (peginterferon alfa-2a) in combination with ribavirin, and/or longer treatment duration, may increase treatment success rates in patients who didn't respond to at least twelve weeks of PegIntron(TM) (peginterferon alfa-2b) plus ribavirin and who didn't discontinue treatment due to haematological adverse events.

The results demonstrated that while a fixed-dose induction did not contribute to treatment success, patients receiving 72 weeks of re-treatment with peginterferon alfa-2a doubled the chance of achieving a cure compared with the previous standard of 48 weeks (16% vs. 8%). Furthermore, the study showed that for the 17% of patients who responded by week 12 (defined as HCV RNA levels of less than 50 IU/mL), 57% went on to achieve a cure after a 72-week treatment course, compared with only 35% of patients who were re-treated for 48 weeks.

"It is a significant step forward that we now know patients who have undetectable levels of hepatitis C at week 12 have a good likelihood of achieving a cure with Pegasys and ribavirin. This ability to predict success after just three months will give both doctors and hepatitis C patients additional confidence when considering whether to re-treat," said Professor Jensen.

Treatment with peginterferon alfa-2a plus ribavirin was well tolerated in the study. The adverse event profile was similar to that seen in patients treated for the first time. Further analyses of the 72-week treatment duration in REPEAT showed that it was associated with a more favourable benefit:risk ratio than 48 weeks of treatment.(3) The most common side effects of treatment were flu-like symptoms, fatigue, depression and haematological abnormalities.

References

- (1) Jenson DM, Marcellin P, Bradley F et al. Re-treatment of chronic hepatitis C non-responders to peginterferon alfa-2b: a randomized trial. *Annals of Internal Medicine* 2009;150(8):528-540.
- (2) Swain M, Lai M, Shiffman M, Cooksley W et al. Sustained virologic response (SVR) resulting from treatment with peginterferon alfa-2a (40KD) (Pegasys(R)) alone or in combination with ribavirin (Copegus(R)) is durable and constitutes a cure: an ongoing 5-year follow-up. Abstract presented at Digestive Disease Week; 21 May 2007; Los Angeles, California, USA.
- (3) Marcellin P. et al. A 72-week treatment duration with peginterferon alfa-2a (40KD) (PEGASYS(R)) plus ribavirin (COPEGUS(R)) has a favorable risk:benefit ratio in non-responders to pegylated interferon alfa-2b (12KD) plus ribavirin: findings of the multinational REPEAT study. Poster (PO1873) presented at Annual Meeting of the American Association for the Study of Liver Diseases (AASLD); 31 October - 4 November 2008; San Francisco, California, USA.

Source: Roche

Vitamin K may boost effects of cancer pill Nexavar

www.reuters.com

CHICAGO (Reuters) - Vitamin K may enhance the effects of the cancer drug **Nexavar**, which may allow patients to take lower, less-toxic doses, U.S. researchers said on Wednesday.

They said combining vitamin K with the cancer pill Nexavar or sorafenib sold by Onyx Pharmaceuticals Inc and German drugmaker Bayer AG helped it kill liver and pancreatic cancer in human cell cultures.

"K vitamins ... appear to enhance the effects of sorafenib, thus requiring lower, less-toxic doses," Dr. Brian Carr of Thomas Jefferson University in Philadelphia said in a statement.

"Many patients need to discontinue treatment with sorafenib because of the debilitating side effects," Carr said. "If we could lower the dose, more patients would be able to complete their treatment."

Nexavar is approved for use in liver kidney cancer and is being tested for an array of other cancers, including melanoma, lung and breast cancer. It had global sales last year of \$678 million.

Carr said combining the drug with vitamin K may help patients avoid hand-foot syndrome, a common side-effect of Nexavar that affects about 20 percent of patients.

It typically causes painful sores on the soles of patients' feet that can prevent the patients from walking, said Carr, who presented his findings from two studies at the American Association for Cancer Research meeting in Denver.

He and colleagues tested both vitamin K1 and vitamin K in combination with sorafenib in pancreatic cell lines. Each combination inhibited cell growth, killed cells and slowed enzymes that promote cancer cell growth.

With vitamin K, the team could use half the normal dose and still slow cancer cell growth. Alone, the lower dose of sorafenib was ineffective.

In the second study, vitamin K1 also enhanced the effects of sorafenib in hepatocellular carcinoma or primary liver cancer.

Vitamin K is found in green, leafy vegetables such as kale, collard greens, broccoli, Brussels sprouts and parsley and is known to play a role in blood clotting and building bones.

(Editing by Maggie Fox and Bill Trott)

Tougher rules planned for N.L. MDs infected with HIV, hepatitis

<http://www.cbc.ca>

Doctors in Newfoundland and Labrador who have particular infectious diseases may soon be limited in the procedures they can perform on patients.

Physicians who contract HIV or hepatitis will also be required to notify the College of Physicians and Surgeons of Newfoundland and Labrador, if proposed changes are adopted.

College registrar Dr. Robert Young was not available for an interview, but a college official confirmed it is proposing that physicians with HIV or hepatitis work with an arm's length committee that could limit a physician's practice, and in the end may prevent that physician from doing riskier procedures.

The Newfoundland and Labrador Medical Association says the college's proposed policy needs work. Executive director Robert Ritter said any mandatory reporting policy must strike a balance between patient safety and protecting physicians' individual rights.

Some provinces, including Alberta, B.C. and Nova Scotia, already have committees that work with infected physicians.

But Dr. Philip Berger, an Ontario physician who treats patients with HIV/AIDS, said such a policy is unfair, because many conditions — such as epilepsy — could affect a physician's ability to practise.

"Unless the college in Newfoundland makes it mandatory to report any condition which could affect a physician's performance, then it is just singling out and discriminating against doctors with HIV or hepatitis B," Berger said.

Berger said a committee-management system could do more harm than good.

"The consequence is stigmatizing or making HIV [or] hepatitis look a lot more dangerous than it actually is," Berger said.

Settlers Life Insurance Denies Claim For Widow Of Gunshot Victim Due To Pre-Existing Medical Condition

<http://consumerist.com>

By Chris Walters

At Settlers Life Insurance, being shot in the back by unknown assailants is trumped by Hepatitis C, and they won't pay your benefits. According to the lawsuit filed last week (pdf), Curtis McCraw held a life insurance policy with Settlers Life Insurance at the time of his murder in April 2008. When his wife Stephanie McCraw attempted to claim the Accidental Death Benefit, Settlers denied her claim because her husband had "a pre-existing liver condition." We knew Hepatitis was bad, but we didn't know it could pull out a gun and shoot you. We wonder if Hepatitis C is what really killed Kennedy.

AVEO Announces Positive Finding For Triple VEGF Receptor Inhibitor AV-951 In Preclinical Model Of Liver Cancer

<http://www.medicalnewstoday.com>

AVEO Pharmaceuticals, Inc., a biopharmaceutical company leveraging breakthrough discoveries in cancer biology to discover, develop and commercialize targeted oncology therapies, today announced data from its proprietary preclinical models which demonstrates that the company's potent and selective triple VEGF receptor inhibitor, **AV-951**, exhibits robust inhibitory activity in its novel, genetically engineered model of hepatocellular carcinoma (HCC), the most common form of liver cancer. These data were presented at the American Association for Cancer Research (AACR) 100th Annual Meeting in Denver, Colorado.

"By utilizing the unique capability of our proprietary cancer biology platform to guide drug development strategies for AV-951, which is currently completing Phase 2 clinical development in advanced renal cell carcinoma, we are able to create more relevant models of human cancer in which to evaluate efficacy," stated Tuan Ha-Ngoc, president and chief executive officer of AVEO Pharmaceuticals. "The activity of AV-951 in AVEO-engineered models of hepatocellular carcinoma highlights the potential role of our novel, triple VEGF receptor inhibitor in the treatment of this deadly cancer."

AVEO generated primary HCC tumors in mice using a previously established tissue reconstitution approach. Mice reconstituted with KRAS/p53- and myc/p53- developed tumors in the liver with a latency of two to five months and penetrance of 30 to 50 percent. Histological examination demonstrated that these tumors resemble the features of human HCCs.

Preclinical data presented at AACR showed variation in vessel histology among primary HCC tumors, and a subset of HCC tumors exhibited microvessels consistent with VEGF driven angiogenesis. AVEO observed activity of its potent, triple VEGF inhibitor AV-951 in these HCC models, suggesting that AV-951 may be an efficacious single-agent treatment for human HCC.

"Recently, one multi-targeted tyrosine kinase inhibitor was able to demonstrate survival benefit in this type of liver cancer. To evaluate whether AVEO's selective VEGF receptor inhibitor may be efficacious in liver cancer, we created and evaluated these engineered HCC models," stated Murray O. Robinson, Ph.D., senior vice president of oncology at AVEO. "We are encouraged by the activity of AV-951 in this model."

About Liver Cancer

Liver cancer is the fifth most common cancer type and the third leading cause of cancer related death worldwide. In the U.S., the number of new cases continues to rise. The most common causes of liver cancer include hepatitis B/C infection, consumption of Aflatoxin B1 contaminated food, and alcohol abuse. The prognosis for most liver cancer patients is extremely poor due to late diagnosis and the five-year overall survival is less than 10 percent. Current treatment options are limited and include surgery, radiation therapy and chemotherapy. Liver cancer can be divided into two subtypes: hepatocellular carcinoma (HCC), which originates from hepatocytes and accounts for 80 to 90 percent of the cases; and adenocarcinoma, which originates from ductal epithelial cells and accounts for the other 10 to 20 percent.

About AV-951

AV-951 is a novel, highly potent and selective inhibitor of VEGF receptors 1, 2 and 3, exhibiting picomolar inhibitory activity against all three receptors. Angiogenesis inhibition has demonstrated benefit for patients with a wide range of cancer types, including renal cell carcinoma, metastatic breast cancer, colorectal cancer, and non-small cell lung cancer. Due to its potency and specificity, AVEO believes AV-951 may enable maximal inhibition of the VEGF pathway, while avoiding side effects associated with off-target activity. Such a profile may enable AV-951 to be more readily combined with standard chemotherapy as well as other targeted therapies, potentially increasing the breadth of its clinical utility. In addition, AVEO has evaluated AV-951 using its Human Response Platform (HRP™), a unique set of engineered tumor models that provide further insight into potential clinical settings, combinability with other anti-cancer agents, tumor subtypes and responsive patient populations.

AVEO is conducting a Phase 2 placebo-controlled, randomized discontinuation trial assessing the efficacy and safety of once-daily, oral AV-951 in renal cell carcinoma (RCC) as well as ongoing Phase 1b trials of AV-951 in combination with temsirolimus, an approved mTOR inhibitor, in patients with mRCC; in combination with the FOLFOX6 chemotherapy regimen in patients with advanced colorectal cancer and other gastrointestinal cancers; in combination with paclitaxel in patients with metastatic breast cancer; and as monotherapy in patients with non-small cell lung cancer.

Source: AVEO Pharmaceuticals, Inc.

Hepatitis B Injection Approved for Treating Acute Exposure

<http://www.docguide.com>

NEW YORK -- April 23, 2009 -- Health Canada has approved the hepatitis B immune globulin (human) injection (HepaGam B) for treating acute exposure to hepatitis B virus (HBV).

Specifically, the approval is for post-exposure prophylaxis (PEP) for acute exposure to blood containing hepatitis B surface antigen (HBsAg), perinatal exposure of infants born to HBsAg-positive mothers, sexual exposure to HBsAg-positive persons, and household exposure to persons with acute hepatitis B infection.

The most common expected adverse drug reactions for intravenous immune globulins are chills, fever, headaches, vomiting, allergic reactions, nausea, arthralgia, and moderate low back pain.

SOURCE: Cangene

Vet Negative For Virus After Retesting

<http://www.wsmv.com>

Reported By Deanna Lambert

Thousands Worried About Health After V.A. Colonoscopy Issues

MURFREESBORO, Tenn. -- A veteran possibly infected with a virus following a colonoscopy at the Murfreesboro Veterans Affairs clinic received a second call informing him that he needed to be retested, and the results were negative.

The man is just one of thousands of vets who have been worried about their health because of equipment problems and protocols at the VA.

The man, who did not want to be identified, went for a third, independent test to find out if he has a disease or not.

"I was in my home, in my kitchen," said the veteran of the Vietnam War. "My wife was present, and it just knocked us down. I mean, I just cried in rage. We held each other."

But the nightmare for the Smith County man did not stop there. The VA called back, saying he needed to be retested.

"They called back about four or five days later after that second test," said the veteran. "And again, it was not in writing, but it was a call, saying, 'You are negative and have nothing to worry about.'"

But with one negative test and one positive test for two very serious and possibly life-threatening diseases, he's still worried and disappointed.

"It leaves me with a feeling that I can't trust the VA medical community," he said. "I am going to get independent testing done for my own peace of mind and that of my wife's, because if I had any of those (illnesses), then my wife does."

"You can imagine the concern and fear and anxiety in these veteran families," said attorney Michael Sheppard, who has been contacted by more than 40 veterans looking for help. "The problem is that the VA is not coming out with how their investigation is progressing."

"There's a lot of unanswered, you know, questions that need to be answered and ... solved before they can move on," said the veteran.

Channel 4 has been unable to confirm what prompted the veteran's retesting and how many others have to be retested. It's also unknown if there are any deaths possibly linked to virus contacted in a colonoscopy.

The VA said three veterans have tested positive for HIV, including one from the York facility in Murfreesboro, and two others in Georgia and Florida. At least 10 other patients at York have tested positive for Hepatitis B and C.

Channel 4 also asked the VA for an update Thursday on those numbers but was told only that the VA is "working on it."

Metabolic Syndrome Hikes Mortality in Hepatitis C

<http://www.medpagetoday.com>

By John Gever, Senior Editor, *MedPage Today*

Reviewed by Robert Jasmer, MD; Associate Clinical Professor of Medicine, University of California, San Francisco

WHEELING, W.Va., April 24 -- Patients with hepatitis C infection appear more likely to die from the condition if they also suffer from one or more components of metabolic syndrome, a researcher said.

Excess body weight and hypertension both significantly heightened the risk of liver-related mortality in hepatitis C patients, according to data from the third National Health and Nutrition Examination Survey (NHANES) series, reported Zobair Younossi, M.D., of Inova Health System in Falls Church, Va.

Those two factors as well as the third component of metabolic syndrome -- type 2 diabetes -- also made death from all causes more likely during the study period, said Dr. Younossi.

He spoke with MedPage Today by telephone from Copenhagen, Denmark, in advance of his formal presentation of the data at the annual meeting of the European Association for the Study of the Liver.

Earlier research had found numerous factors associated with more rapid progression of hepatitis C infection, Dr. Younossi said, including components of metabolic syndrome individually and, perhaps, together.

To explore the relationship, Dr. Younossi and his colleagues analyzed data from NHANES III, conducted from 1988 to 1994. The data also include mortality follow-up information through 2000, a median of 8.5 years.

Out of more than 31,000 NHANES participants, the researchers identified 264 with hepatitis C and 13,004 without liver disease who could serve as controls.

Only survey participants with complete records for numerous clinical parameters were eligible for inclusion in the study.

The researchers found that hepatitis C cases were more likely than controls to have insulin resistance, as defined by a HOMA score of at least 3 -- 37.4% of cases versus 22.5% of controls (P=0.02) -- and were dramatically more likely to smoke (64.0% versus 26.6%, P<0.001).

A diagnosis of type 2 diabetes was moderately more common among cases as well.

On the other hand, the hepatitis C cases showed somewhat lower rates of hypertension, obesity, and metabolic syndrome.

But the 51 deaths among the hepatitis C cases were disproportionately concentrated in those with

the latter conditions.

With multivariate analysis, the researchers calculated the following adjusted hazard ratios for all-cause mortality in hepatitis C cases, compared with controls:

- Type 2 diabetes: HR 2.14 (95% CI 2.11 to 2.16)
- Higher body mass index: HR 1.05 (95% 1.05 to 1.06)
- Hypertension: HR 1.41 (95% CI 1.39 to 1.42)

For liver-related death only, two of these three factors were also strong predictors in the hepatitis C cases:

- Higher BMI: HR 1.28 (95% CI 1.27 to 1.28)
- Hypertension: HR 3.75 (95% CI 3.65 to 3.85)

Dr. Younossi said that patients with any of the components of metabolic syndrome should be treated for them, and those with hepatitis C are no exception.

But he cautioned that only a prospective trial could confirm that successful treatment of metabolic syndrome or its components would improve survival in hepatitis C patients.

He also noted several limitations of the study: lack of liver biopsy or genotype data for hepatitis C cases, a relatively short follow-up, and the potential underestimation of hepatitis C prevalence in NHANES data.

LVADs can cause false-positive HCV-antibody tests, diligent follow-up testing urged to preserve transplant eligibility

<http://www.theheart.org>

Steve Stiles

Paris, France - Someone awaiting heart transplantation who is fitted with a **left ventricular assist device (LVAD)** may be at increased risk of falsely testing positive for hepatitis C virus (HCV) antibody, according to a study that included only a handful of patients but highlights the importance of more definitive follow-up testing to confirm or, preferably, rule out HCV infection [1].

The stakes could be high, in that, at most institutions, HCV infection would render the patient a marginal candidate for transplantation or even ineligible for a new heart, although, as Dr Ajay V Srivastava (Henry Ford Hospital, Detroit, MI) pointed out for heartwire, there are few if any guidelines on the question, and it's unclear how HCV testing protocols may differ from center to center.

In his group's series of 23 patients who tested negative for HCV before receiving LVADs for bridging to transplantation, seven tested positive within two weeks of device implantation, Srivastava reported here at the International Society for Heart and Lung Transplantation 2009 Scientific Sessions.

Repeat serologic testing followed as needed by the more discriminating radio immunoblot assays

(RIBA) and HCV polymerase chain reaction (PCR) RNA-amplification tests ultimately ruled out actual HCV infection in every case.

Thirteen of the patients had been implanted with pulsatile Heartmate XVE devices and 10 received the continuous-flow Heartmate II (Thoratec, Pleasanton, CA); the type of device had no apparent effect on HCV test results in the study, Srivastava said.

His group recommends repeat serologic testing for transplant candidates with LVADs who at any point test positive for HCV, followed as necessary for those with persisting positive results by progressively more definitive tests "in order to prevent undue alarm among patients and to prevent candidates from being denied transplantation and to facilitate a diagnosis if the patient has HCV," Srivastava said.

"It's unclear whether other centers are using these sequential tests, but we think they should be performed in every patient [who initially tests positive for HCV]."

The findings highlight what little is known about the generalized immune and inflammatory responses elicited by LVAD support and the surgery to put the device in place. Many LVAD recipients, Srivastava observed, develop anti-human-leukocyte-antigen (anti-HLA) antibodies, probably from the large volume of blood products typically received when the device is implanted. Reactions to the LVAD hardware itself and generalized responses to bacterial infections may also contribute to incorrect results at HCV serologic testing.

HCV-antibody testing was performed in all patients at two, four, and eight weeks after LVAD implantation. Of the seven patients who tested positive at some point, two subsequently became serologically negative.

The more discriminating tests were then performed in the five patients with persisting positive tests. None showed detectable levels of the virus at PCR testing. Two were HCV-negative and three were indeterminate by RIBA.

Interestingly, the pattern of RIBA antibody detection was the same for all three indeterminate tests: they involved antibodies to 5-1-1p/c100 peptide but not to the peptides c33p, c22p, NS5, or hSOD.

According to Srivastava, why some of the patients would have indeterminate RIBA results and why those results would involve one particular peptide to the exclusion of others remains unknown. But the finding may have some clinical relevance, he observed. Among nontransplant patients receiving blood transfusions who initially test positive for HCV, those who are positive for the c100 peptide "usually turn out to be false positives, whereas patients who have antibodies to the c33 and the other peptides turn out to have the hepatitis C virus."

NJ authorities looking for source of hepatitis C

<http://www.philly.com>

The Associated Press

ATLANTIC CITY, N.J. - Health officials are trying to determine the source of 15 cases of

hepatitis C reported by an Atlantic City hospital.

The cases at AtlantiCare Regional Medical Center date back as far as 2005.

Those stricken are patients at the hospital's dialysis unit. But health officials say they do not know whether the cases are linked to the hospital.

Hepatitis C attacks the liver and can be fatal.

The state says that in 2007, there were more than 100 acute cases and more than 7,000 chronic cases statewide.